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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/813,589 | 03/21/2001 | Stephen A. Goff | S-20359D | 1510 |

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| EXAMINER | |
|---|---|
| WOITACH, JOSEPH T | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1632 | 3 |

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Please find below and/or attached an Office communication concerning this application or proceeding.

File

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/813,589 | GOFF ET AL. | |
| | Examiner | Art Unit | |
| | Joseph T. Woitach | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *26,28-35 and 37-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *26,28,29,31-35 and 37-41* is/are rejected.

7)☐ Claim(s) *30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

This application is a continuation of Application 09/625,904, filed July 26, 200, now abandoned, which is a continuation of Application 9/234,190, filed 1/20/1999, which is a division of Application 9/010,050, filed 1/21, 1998, now patent 5,880,333, which is a continuation of application 8/398,037, filed 3/3/1995, abandoned.

The preliminary amendment filed March 21, 2001, paper number 3, has been entered. The specification has been entered. Claims 1-25, 27 and 36 have been canceled. Claims 26, 28, 31 and 32 have been amended. Claims 37-41 have been added. Claims 26, 28-35 and 37-41 are pending and currently under examination.

### *Sequence Compliance*

Applicants request to transfer the sequence listing in parent application 09/625,904, has been processed and entered (paper number 2). The instant application is in sequence compliance.

### *Information Disclosure Statement*

The information disclosure statement filed March 21, 2001, attachment to paper number 2, indicates that the listed references are provided in parent application 09/625,904. Upon review of the file of application 09/625,904 Examiner has indicated the references which were provided

in the parent application. It is noted that the Tomlin (AA3) reference has been provided with the instant filing.

***Abstract***

The abstract of the disclosure is objected to because it contains legal phraseology such as "means" and "said"

Appropriate correction is required. See MPEP § 608.01(b).

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 41 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. If a transgenic plant is hemizygous for the recited transgene, then either 50% or 25% of the seed it produces would lack the transgene, depending on whether the plant is cross- or self-pollinated. Therefore, the claims would encompass unmodified seeds, which are a 'product of nature' and not statutory matter. This rejection could be overcome by amending the claim to recite that the seed retains the transgene.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40 and 41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 40 and 41 encompass any plant and seed which comprises the expression cassette of claim 26. Claim 26 recites a receptor expression cassette for use in controlling gene expression comprising: a) a 5' regulatory region capable of promoting expression in a plant cell; b) an operably linked encoding a receptor polypeptide which is a member of the Class II steroid superfamily of nuclear receptors; and c) a 3' terminating sequence, and is broadly drawn to any promoter controlling the expression of the expression cassette and any receptor of the Class II steroid/thyroid superfamily receptors besides those which were specifically evaluated for function in individual plant cells. The specification is silent with respect to methods of obtaining whole plants, or seed therefrom containing said expression cassette, or the evaluation and obtention of controlled expression and function of the expression cassette in whole transgenic plants. Further, as claim 26 is written and as claimed in later dependent claims, the receptor

polypeptide can comprise any combination of DNA binding domains and ligand binding domains from any Class II steroid/thyroid hormone nuclear receptor superfamily.

The controlled, receptor gene-mediated expression of target genes in transgenic plants is unpredictable as evidenced by Lloyd *et al.* who teach that a full-length receptor which was effective in transformed plant cells and yeast was unable to effect target gene expression in whole plants (page 439; bottom paragraph of first column), and that different receptors resulted in less efficient control with varying levels of background expression (page 436; bottom paragraph of first column). Lloyd *et al.* teach that multicellular, multi-tissued plants are complex organisms, wherein the expression of a single gene may be insufficient to produce a desired phenotype when taken with other factors such as the expression of *ttg* and the effect of R and C1 in maize (page 436; second paragraph). Furthermore, the design, production and evaluation of receptor genes encoding chimeric receptors which are still able to function in plant cells and whole plants is unpredictable as evidenced by Lloyd *et al.* (page 439; bottom of first column) and the instant specification (page 11; lines 23-28). In addition, the expression of chimeric receptors may already confound an already complex system wherein the ligand binding domain may bind undesired or endogenous ligands, and so prevent the controlled activation of transcription and expression of the desired target gene, or reduce its selective induction (instant specification page 11; lines 7-12). Therefore, while the specification provides working examples of specific receptor constructs which work in plant cells, it does not provide the guidance necessary to

demonstrate a nexus between this expression and the unpredictability of expression and function in whole plants.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required one of skill in the art undue experimentation to practice the invention as claimed.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26, 28, 29, 31 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schena *et al.* in view of Koelle *et al.* and Christopherson *et al.*

Claims 26, 28, 29, 31, 32 and 37-39 encompass a receptor expression cassette comprising: a) a 5' regulatory region capable of promoting expression in a plant cell; b) an

operably linked encoding a receptor polypeptide which is a member of the Class II steroid superfamily of nuclear receptors; and c) a 3' terminating sequence. Dependent claims recite that the receptor polypeptide comprises the Ecdysone receptor, a heterologous transactivation domain, a heterologous DNA binding domain (in particular the GAL4 protein) and that said receptor expression cassette be contained in a plant transformation vector. Schena *et al.* teach a receptor expression cassette which encodes the glucocorticoid receptor for the inducible control expression of a target gene in plant cells (entire document), however the glucocorticoid receptor is a Class I steroid nuclear receptor. Koelle *et al.* teach the gene encoding the ecdysone receptor and compare it to previously characterized Class II steroid nuclear receptor super family (page 61; middle of first column and figure 2). Further, it is demonstrated both *in vitro* and in cell culture that the ecdysone receptor can be expressed and used to drive a heterologous reporter gene construct (figure 5 and figure 7, respectively). Christopherson *et al.* teach the ecdysone receptor and chimeric transactivators substituting different activation, DNA binding and ligand binding domains to study their ability to respond to different ligands and activate different promoters constructs (entire document and summarized on page 6316; figure 2). Further, Christopherson *et al.* teaches that one can substitute domains from other proteins such as GAL4 and VP16 (page 6318; first column and figure 2, respectively). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the ecdysone receptor and chimeric transactivating receptor constructs for the glucocorticoid receptor in the expression cassette taught by Schena *et al.* One having ordinary

skill in the art would have been motivated to substitute these receptors, one for the other, in order to obtain inducible gene expression systems suitable for use in higher plants (Schena page 10422; first paragraph and page 10424; first paragraph of discussion). There would have been a reasonable expectation of success given the results of Koelle *et al.* and Christopherson *et al.* demonstrating the versatility of the ecdysone receptor and chimeric transactivators in different systems with different promoters to use these Class II steroid nuclear receptors in the plant receptor expression system described by Schena *et al.* to optimize and increase the efficiency of inducible expression systems in plants.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Claims 26, 33, 34 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schena *et al.* in view Evans *et al.* (WO94/01558).

Claims 26 and 37-39 are summarized above. Claims 33 and 34 are dependent claims which encompass a receptor cassette encoding ultraspiracle receptor (USP) and USP which comprises a heterologous transactivation domain. Schena *et al.* teach a receptor expression cassette which encodes the glucocorticoid receptor for the inducible control expression of a target gene in plant cells (entire document). Evans *et al.* teach the gene encoding the USP receptor, which is a member of the Class II steroid/thyroid nuclear receptor super family, and chimeric USP receptors (entire document and summarized on page 4; lines 25-37). Further, it is demonstrated that USP can function *in vitro* and *in vivo* (pages 34-39; Examples VII and VIII) .

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the USP receptor and chimeric transactivating receptor constructs for the glucocorticoid receptor in the expression cassette taught by Schena *et al.* One having ordinary skill in the art would have been motivated to substitute these receptors, one for the other, in order to obtain inducible gene expression systems suitable for use in higher plants (Schena page 10422; first paragraph and page 10424; first paragraph of discussion). There would have been a reasonable expectation of success given the results of Evans *et al.* demonstrating the versatility of the USP receptor and chimeric transactivators in different systems with different promoters to use these Class II steroid nuclear receptors in the plant receptor expression system described by Schena *et al.* to optimize and increase the efficiency of inducible expression systems in plants.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schena *et al.* in view Evans *et al.* as applied to claims 26, 33, 34 and 37-39 above, and further in view of Christopherson *et al.*

Claims 26, 33, 34 and 37-39 are summarized above. Claim 35 encompasses a receptor cassette of claim 34 wherein said heterologous transactivation domain is from VP16. Schena *et al.* in view Evans *et al.* teach an expression cassette comprising the USP receptor and chimeric transactivating receptor constructs for the glucocorticoid receptor. However, they do not teach

specifically to substitute the VP16 transactivating domain into the chimeric transactivating receptor constructs. Christopherson *et al.* teach chimeric transactivators substituting different activation, DNA binding and ligand binding domains to study their ability to respond to different ligands and activate different promoters constructs, in particular that one can substitute the transactivating domain of VP16 in chimeric constructs (entire document and summarized on page 6316; figure 2). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the VP16 transactivating domain into the transactivating receptor constructs into the expression cassette taught by Schena *et al.* and Evans *et al.* One having ordinary skill in the art would have been motivated to substitute these receptors, one for the other, in order to obtain inducible gene expression systems suitable for use in higher plants (Schena page 10422; first paragraph and page 10424; first paragraph of discussion). There would have been a reasonable expectation of success given the results of Christopherson *et al.* demonstrating the versatility of the VP16 transactivating domain in various chimeric transactivator constructs in different systems with different promoters to use this nuclear receptor in the plant receptor expression system described by Schena *et al.* and Evans *et al.* to optimize and increase the efficiency of inducible expression systems in plants.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

***Conclusion***

No claim is allowed.

Claim 30 is free from the art of record in view of the prior art to teach or suggest the claimed combination of C1 regulatory gene of maize with other receptor gene domains under the control of a plant promoter. Claim 30 is objected to as being dependent upon a rejected claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

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